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GYNECOLOGY

Uncovering changes in proteomic signature of rat pelvic floor muscles in pregnancy

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Background

Structural and functional changes of the rat pelvic floor muscles during pregnancy, specifically, sarcomerogenesis, increase in extracellular matrix content, and higher passive tension at larger strains protect the integral muscle components against birth injury. The mechanisms underlying these antepartum alterations are unknown. Quantitative proteomics is an unbiased method of identifying protein expression changes in differentially conditioned samples. Therefore, proteomics analysis provides an opportunity to identify molecular mechanisms underlying antepartum muscle plasticity.

Objective

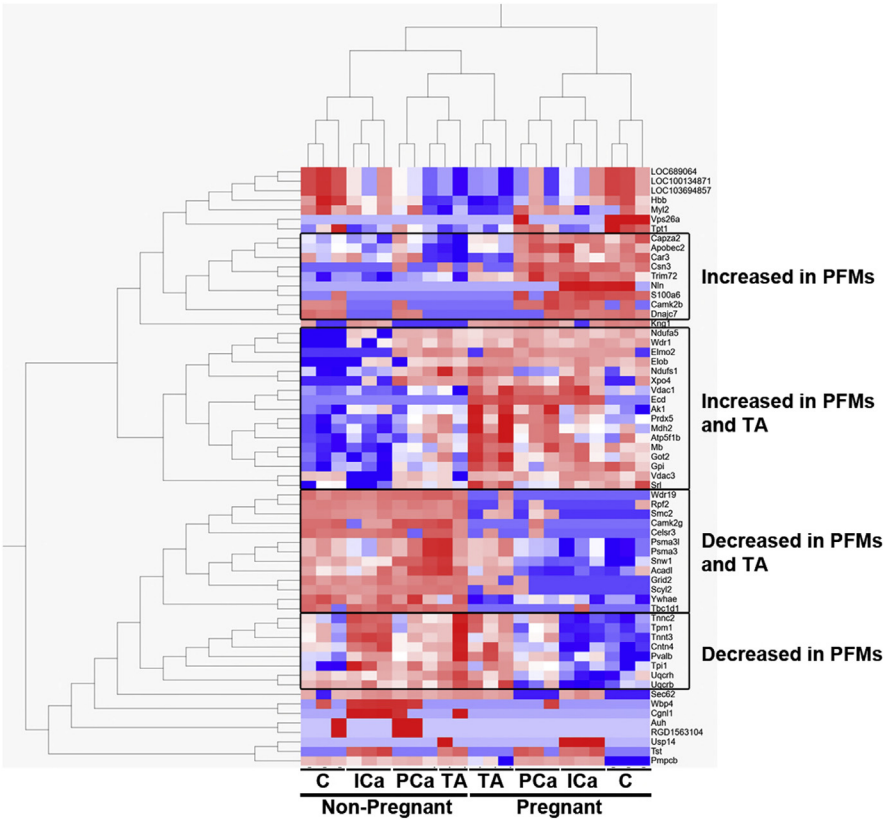
To elucidate putative mechanisms accountable for pregnancy-induced adaptations of the pelvic floor muscles, and to identify other novel antepartum alterations of the pelvic floor muscles.

Materials and Methods

Pelvic floor muscles, comprised of coccygeus, iliocaudalis, and pubocaudalis, and nonpelvic limb muscle, tibialis anterior, were harvested from 3-month-old nonpregnant and late-pregnant Sprague-Dawley rats. After tissue homogenization, trypsin-digested peptides were analyzed by ultra-high-performance liquid chromatography coupled with tandem mass spectroscopy using nano-spray ionization. Peptide identification and label free relative quantification analysis were carried out using Peaks Studio 8.5 software (Bioinformatics Solutions Inc., Waterloo, ON, Canada). Proteomics data were visualized using the Qlucore Omics Explorer (New York, NY). Differentially expressed peptides were identified

FIGURE

Heat map of tryptic digest peptides from rat pelvic floor muscles (PFMs) and tibialis anterior (TA)



Heat map demonstrating 4 major gene clusters (black boxes). Cluster 1: proteins increased in pregnancy only in PFMs. Cluster 2: proteins increased in in pregnancy in both PFMs and TA. Cluster 3: proteins decreased in pregnancy in both PFMs and TA. Cluster 4: proteins decreased in pregnancy only in PFMs. Colors represent relative quantification of protein abundance in $\log^2$ intensity scale, with blue indicating the lowest and red the highest protein expression. Gene names encoding differentially expressed proteins are listed on the right side of the heatmap.

C, coccygeus; *ICa*, iliocaudalis; *PCa*, pubocaudalis.

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using the multi-group differential expression function, with q-value cutoff set at <0.05. Proteomic signatures of the pelvic floor muscles were compared to nonpelvic limb muscle and between nonpregnant and pregnant states.

Results

Unsupervised clustering of the data showed clear separation between samples from nonpregnant and pregnant animals along principal component 1 and between pelvic and nonpelvic muscles along principal component 2. Four major gene clusters were identified segregating proteomic signatures of muscles examined in nonpregnant vs pregnant states: (1) proteins increased in the pelvic floor muscles only; (2) proteins increased in the pelvic floor muscles and tibialis anterior; (3) proteins decreased in the pelvic floor muscles and tibialis anterior; and (4) proteins decreased in the pelvic floor muscles alone. Cluster 1 included proteins involved in cell cycle progression and differentiation. Cluster 2 contained proteins that participate in mitochondrial metabolism. Cluster 3 included proteins involved in transcription, signal transduction, and phosphorylation. Cluster 4 comprised proteins involved in calcium-mediated regulation of muscle contraction via the troponin tropomyosin complex (Figure).

Conclusion

Pelvic floor muscles gain a distinct proteomic signature in pregnancy, which provides a mechanistic foundation for the antepartum physiological alterations acquired by these muscles. Variability in genes encoding these proteins may alter plasticity of the pelvic floor muscles and therefore the extent of the protective pregnancy-induced adaptations. Furthermore, pelvic floor muscles' proteome is divergent from that of the nonpelvic skeletal muscles. ■

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